

# A Prospective Study on Patterns of Hepatic Involvement in Dengue Infection

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Received: October 2020

Accepted: October 2020

## ABSTRACT

**Background:** DENV (dengue viral infection) is a non-hepatotropic RNA virus, but hepatic involvement is common. High level of viremia is associated with involvement liver and other organs. Present study is a prospective study which is aimed to know about the, pattern of hepatic involvement in dengue patients admitted in General Medicine Dept Konaseema Institute of Medical Science. **Methods:** This is a prospective hospital-based study conducted in the Department of General Medicine Konaseema Institute of Medical Science Amalapuram Andhra Pradesh, from December 2015 to December 2017. During two year of study period 126 clinically and serologically positive patients of Dengue fever, Dengue haemorrhagic fever and Dengue shock syndrome, classified as per the, definition of national vector borne disease control programme Govt. of India. **Results:** Mean value of total bilirubin was 0.8 mg/dl in DF patients, 0.96mg/dl in DHF patients and 1.08mg/dl in DSS patients. Mean value of AST was 77.44(IU/L) in DF group, 112.32 IU/L in DHF group and 486.28 in DSS group. In DF group mean ALT in DHF group was 94.36 (IU/L) and it was 386.42 IU/L in DSS group. Mean value of serum albumin was 3.97 gm/dl in DF group, 3.65 gm/dl in DHF group and 3.49 gm/dl in DSS group. Serum globulin mean value was 2.98mg/dl in DF group, 2.86 gm/dl in DHF group and 2.69 gm/dl in DSS group. Serum alkaline phosphate level was also increased in all the groups, mean value of ALP was 118.46 IU/L in DF group, 164.32 IU/L in DF group, 164.32 IU/L in DHF patients and 342.42 IU/L in DSS group. **Conclusion:** The pattern of hepatic involvement of liver in dengue fever varies as per the severity of disease. In milder case of dengue fever liver function test was normal but there was hepatomegaly was present commonly but in severe form of disease pattern of hepatic involvement varies from tender hepatomegaly to significant increase in liver enzyme.

**Keywords:** Coastal Andhra Pradesh, Dengue fever, Hepatic dysfunction.

## INTRODUCTION

Dengue is a mosquito born viral infection and is most common cause of arboviral disease in tropical and subtropical region. Four types of dengue virus exists DEN1, DEN2, DEN3 and DEN4, immunity to this is type specific so that it is possible for person to have four separate episodes of dengue fever.<sup>[1,2]</sup> At present DEN1, DEN2 and DEN3 is wide spread in India. Dengue has been classified in to

- Dengue fever (DF) which is characterised by fever with least two of these features, muscle or joint pain, cutaneous rashes, ocular pain, headache, leucopenia and bleeding manifestation.
- Dengue haemorrhagic fever, thrombocytopenia ( $<100 \times 10^9/L$ ) bleeding manifestation and plasma leakage.
- Dengue shock syndrome- it is clued dengue haemorrhagic fever with ↑HR, low pulse pressure, hypotension.<sup>[3,4]</sup>

DENV (dengue viral infection) is a non-hepatotropic RNA virus, but hepatic involvement is common. High level of viremia is associated with involvement

liver and other organs. Pathogenesis of liver injury may be due to direct involvement of Hepatocytes and Kuffer cells which is prime target of DENV or, immune mediated damage of liver cells. Mechanism of immune mediated damage to hepatic cells is not clear it may be associated with T-cell activation and cytokine strome.<sup>[5,6]</sup>

Present study is a prospective study which is aimed to know about the, pattern of hepatic involvement in dengue patients admitted in general medicine dept Konaseema Institute of Medical Science.

## MATERIALS AND METHODS

This is a prospective hospital-based study conducted in the department of general medicine Konaseema institute of medical science Amalapuram Andra Pradesh, from December 2015 to December 2017. In present study all clinically suspected dengue infection patients as well as proved by serology and also based on inclusion and exclusion criteria was enrolled for this study.

### Inclusion criteria

- Age above 14yrs, Both sex,
- Serologically and clinically proved cases of DF, DHF and DSS.

### Exclusion criteria

- Existing liver disease.

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- History of hepatotoxic drug intake.
- Diabetic and hypothyroidism patients.

Size of sample was calculated based on prevalence of hepatic involvement in various studies, and expected proportion by using on line calculator for designing clinical research sample-size net and was calculated to be 73.

During two year of study period 126 clinically and serologically positive patients of Dengue fever, Dengue haemorrhagic fever and Dengue shock syndrome, classified as per the, definition of national vector borne disease control programme Govt. of India.<sup>[7]</sup>

Blood sample of all the patients were collected as per routine management protocol and various parameters related to hepatic involvement were studied.

Proper histories of all patients were taken including haemorrhagic manifestation and hypovolemic shock. For screening of patients NS1, ELISA and Dengue specific IgM and IgG antibodies by Ig M and IgG capture ELISA was used. For evaluation of Hepatobiliary function liver enzyme estimation, Alanine transaminase (ALT) Aspartate transaminase (AST), Alkaline phosphatase serum albumin, serum globulin, Total unconjugated and conjugated bilirubin was done, urine examination was done TLC, DC, and platelet count was done in all patients serum urea and creatinine was also done. For all these estimation sysmese KX-21 CBP analyser, Erba EM 200 fully automated and turbo chem 100 fully automated analyzer was used by the dept. of pathology and Biochemistry, Konaseema institute of medical science Amalapuram.

Before start of this study permission from institutional ethics committee was obtained. A written informed consent was also obtained from all those patients enrolled in this study.

#### Statistical analysis

Data were collected and were compiled on Microsoft excel and analysis was done by using, mean, portions and chi-square test ( $\chi^2$ )

## RESULTS

Out of 126 patients with DENV (dengue viral infection) infection were calcified into three groups, 76 patients were having Dengue fever (DF), 30 were diagnosed to be dengue haemorrhagic fever (DHF) and 20 patients having dengue shock syndrome (DSS).

**Table 1: Age and sex distribution of patients.**

| Parameters              | DF<br>(N=76) | DHF<br>(N=30) | DSS<br>(N=20) |
|-------------------------|--------------|---------------|---------------|
| Age (in years) 14-20yrs | 26           | 8             | 6             |
| 21-40yrs                | 40           | 12            | 8             |
| >40yrs                  | 10           | 10            | 6             |
| Sex M:F                 | 1:1          | 1:1.2         | 1:0.8         |

As per [Table 1] among dengue fever (DF) patients 26 patients were between 14 to 20 yrs of age group, 40 patients were between 21 to 40 yrs of age and rest were above 60 yrs of age. In DHF group there were 8 patients between 14 to 20 yrs of age, 12 patients were between 21 to 40 yrs of age rest were above 40yrs of age. In DSS group 6 patients were between 14 to 20yrs of age, 8 patients were between 21 to 40 yrs of age and rest were above 40yrs. In DF group male to female ratio was 1:1 in DHF group this was 1:0.8 and DSS it was 1:1.8.

**Table 2: Clinical presentation of the patients.**

| Parameters         | DF n=76     | DHF n=30    | DSS n=20  |
|--------------------|-------------|-------------|-----------|
| Fever              | 76 (100%)   | 30 (10%)    | 20 (100%) |
| Pain abdomen       | 42 (55.26%) | 12 (40%)    | 11 (55%)  |
| myalgia            | 48 (66.66%) | 18 (60%)    | 9 (45%)   |
| Headache           | 36 (50%)    | 16 (53.3%)  | 11 (55%)  |
| Joint pain         | 42 (55.26%) | 8 (26.6)    | 2 (10%)   |
| Bleeding           | 0 (0%)      | 4 (13.3)    | 6 (30%)   |
| Hepatomegaly       | 18 (25%)    | 18 (60%)    | 18 (90%)  |
| Hepatic tenderness | 4 (5.5%)    | 12 (40%)    | 14 (70%)  |
| Jaundice           | 1 (1.3%)    | 3 (10%)     | 6 (30%)   |
| Petechiae/purpura  | 0 (0%)      | 19 (63.33%) | 13 (65%)  |
| Convulsion         | 0 (0%)      | 0 (0.1%)    | 2 (10%)   |
| Altered sensorium  | 0 (0%)      | 0 (0.1%)    | 1 (5%)    |

As per [Table 2] all the patients are three groups were presented with fever. Out of severity six DF patients forty two patients presented with pain abdomen.

Out of 76 patients of DF 48 presented with myalgia, 12 of out of 30 pt of DHF and 11 out of 20 of DSS were presented with myalgia. 50% of the patients in DF have headache. In 53.3% of DHF patients have headache, and 55% of DSS patients have, headache. Joint pain was found in 55.26% of the DF patients, 26.6% of the patient DHF have joint pain, 10% of DSS patient have same complain. Bleeding manifestation was present in 30% of DSS patient, 13.3% of DHF but absent in DF patients.

**Table 3: Liver function test of dengue patients.**

| Parameters                     | DF<br>(mean) | DHF<br>(mean) | DSS<br>(mean) |
|--------------------------------|--------------|---------------|---------------|
| Total bilirubin (Mg/dl)        | 0.8          | 0.96          | 1.08          |
| Mean AST (IU/L)                | 72.44        | 112.32        | 486.28        |
| Mean ALT (IU/L)                | 66.47        | 94.36         | 386.42        |
| Serum albumin (Mean)           | 3.97         | 3.65          | 3.49          |
| Serum globulin Mg/dl<br>(Mean) | 2.98         | 2.86          | 2.69          |
| ALP (IU/L)                     | 118.46       | 164.32        | 342.42        |

Hepatomegaly and tenderness was common in DSS patients that is 70% same thing was present in 60% and 40% in DHF. Hepatomegaly was present in 25% DF patients. Jaundice was common presentation in DSS that is in 30%. 10% of DHF patient presented

with jaundice but only one patient in DF have jaundice.

In present study Petechiae and purpura was present DHF and DSS patients, absent is DF patients. Convulsion and altered sensorium was present in 10% and 5% patients in DSS but absent in DHF and DF patients.

As per [Table 3] mean value of total bilirubin was 0.8 mg/dl in DF patients, 0.96mg/dl in DHF patients and 1.08mg/dl in DSS patients. Mean value of AST was 77.44(IU/L) in DF group, 112.32 IU/L in DHF group and 486.28 in DSS group. In DF group mean ALT in DHF group was 94.36 (IU/L) and it was 386.42 IU/L in DSS group.

Mean value of serum albumin was 3.97 gm/dl in DF group, 3.65 gm/dl in DHF group and 3.49 gm/dl in DSS group. Serum globulin mean value was 2.98mg/dl in DF group, 2.86 gm/dl in DHF group and 2.69 gm/dl in DSS group. Serum alkaline phosphate level was also increased in all the groups, mean value of ALP was 118.46 IU/L in DF group, 164.32 IU/L in DF group, 164.32 IU/L in DHF patients and 342.42 IU/L in DSS group.

**Table 4: Haematological parameters in dengue fever.**

| Parameters                   | DF    | DHF   | DSS   |
|------------------------------|-------|-------|-------|
| Platelet count (lakhs/cu.mm) | 1.89  | 0.5   | 0.18  |
| Mean of % Lymphocyte count   | 62    | 72    | 70    |
| Mean % Neutrophil count      | 28    | 24    | 26    |
| HB% (gm/dl)                  | 14.26 | 13.28 | 14.62 |

As per [Table 4] regarding haematological parameters, mean value of platelet count was, 1.89 lakhs/cu mm in DF group, 0.50 lakh/cu mm in DHF group and 0.18Lakh/cu mm in DSS patients, the mean% lymphocyte count was 62 in DF, mean% lymphocyte count was 72 in DHF and 70 in DSS patients. Mean of % of neutrophil was 28 in DF, 24 in DHF and 26 in DSS pts. Mean of HB% was 14.26gm/dl in DF patients, 13.28 gm/dl in DHF patients and 14.62 gm/dl in DSS patients.

As per [Table 5] regarding severity of Dengue Fever with respect to liver enzyme we have found that most of the patient in DHF and DSS group have elevated enzyme level and was significant statistically and have p value Less than 0.00001.

**Table 5: Comparison of liver enzyme with respect to severity of dengue.**

| Variables  | Types | Value |        |         | P value   |
|------------|-------|-------|--------|---------|---|
| AST (IU/L) | DF    | 5-40  | 41-200 | 201-400 | >400<br>Chi-square statistic<br>(χ <sup>2</sup> ) |
|            |       | 24    | 47     | 4       | 7   |
|            | DHF   | 7     | 11     | 8       | χ <sup>2</sup> =44.7233                           |
|            | DSS   | 2     | 4      | 6       | P <0.000001                                       |
| ALT (IU/L) | DF    | 20    | 51     | 4       | Chi-square statistic (χ <sup>2</sup> )            |
|            | DHF   | 1     | 16     | 12      | =55.1171, p value                                 |
|            | DSS   | 1     | 3      | 11      | <0.000001   |

**Table 6: Relations between liver function test and hepatomegaly.**

| Parameters (mean)       | Without hepatomegaly, N=72 | With Hepatomegaly, N=54 | P value    |
|-------------------------|----------------------------|-------------------------|------------|
| AST (IU/L)              | 118.62                     | 284.62                  | P <0.00001 |
| ALT (IU/L)              | 96                         | 104.0                   | 0.7751     |
| ALP (IU/L)              | 106.42                     | 121.5                   | >0.05      |
| Serum Albumin (gm/dl)   | 3.2                        | 3.4                     | >0.05      |
| Serum globulin (gm/dl)  | 3.00                       | 2.98                    | >0.05      |
| Total bilirubin (gm/dl) | 0.82                       | 0.96                    | >0.05      |

As per Table 6 regarding relation between liver function test and hepatomegaly, only there is significant difference between AST level in two groups, rest other parameters have no significant difference.

## DISCUSSION

Dengue virus infection is a major public health problem and it has potential fetal complication. Hepatic dysfunction is one of the major manifestations of that complication. Present study has been designed to know the pattern of hepatic involvement in Dengue patient in coastal Andhra Pradesh.

In present study we have found that common age of patient admitted to our hospital were between 20 to 40 yrs of age, and both sexes were equally affected, and DF was the most common presentation followed by DHF and DSS.

As per the study of Yukti Sharma et al 8 below 20yrs age group people was more commonly effected,

which does not corroborate with our study, similarly Krunal D Mehta et al found dengue fever were more common below 30yrs of age, which partially support our study but the study of Gupta E et al supports our study as per him confirm cases of dengue was maximum above 20yrs of age.<sup>[9,10]</sup>

Frequency of DF was more in male then female, but the seriousness of disease was more in female, this supported by the work of Chakrawarti et al and Guha- sapir et al.<sup>[11,12]</sup>

Clinical presentation was similar to the study of Guha- Sapir et al, Rao A and Aswini et al.<sup>[12-14]</sup> Clinical sign of hepatic involvement was more in DHF and DSS group then DF group, this finding is corroborated with the finding Seneviratne SL et al, Bandyopachayay et al and Trung DT.<sup>[15-17]</sup>

Authors have found that the liver enzyme was increased in DHF and DSS group, but it was high in DSS then DHF. We have also found that AST was increased more than ALT. ALP was also increased and serum albumin was toward lower level in severe

patients. All these finding is supported by the study of Bandyopadhyary et al and Shukla V, Chandra A et al.<sup>[16,18]</sup>

Authors have also found that there is significant association between increased liver enzyme and severity of dengue infection, having P value <0.000001, So Hepatic dysfunction is associated with severity of dengue infection. This finding is supported by the finding of Wong M et al and Souza et al.<sup>[19,20]</sup>

In present study we have found that in tender hepatomegaly patient AST was significantly higher than non-tender hepatomegaly patient, but rest of the liver function test was not significantly different, which partially supported by the study of Bandyopadhyary et al and Kalenhalli et al.<sup>[16,22]</sup>

## CONCLUSION

In present study we conclude that pattern of hepatic involvement of liver in dengue fever varies as per the severity of disease. In milder case of dengue fever liver function test was normal but there was hepatomegaly was present commonly but in severe form of disease pattern of hepatic involvement varies from tender hepatomegaly to significant increase in liver enzyme. So, in addition malaria dengue is also presenting with fever, hepatomegaly and increased liver enzyme.

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**How to cite this article:** Kaushik G. A Prospective Study on Patterns of Hepatic Involvement in Dengue Infection. Ann. Int. Med. Den. Res. 2020; 6(6):ME07-ME10.

**Source of Support:** Nil, **Conflict of Interest:** None declared